Remarks

THE AMENDMENTS AND REASONS FOR AMENDMENTS

Applicant cancels claims 21 through 83 and submits new claims 84 through 149. The amendments add no new subject matter and are fully supported throughout the specification including the drawings and the claims as filed.

The amendments are made to clarify the claimed invention and to expedite the allowance of the present application. Applicant reserves the right to file later applications claiming the benefit of priority to the present application.

Support for Amendments

New claims 84-107 correspond to canceled claims 21-44. New claims 110- 116 correspond to canceled claims 46-52. New claims 118- 141 correspond to canceled claims 53-76. New claims 144-149 correspond to canceled claims 78-83.

New independent claim 84, which recites a recombinant cell that comprises a first nucleic acid molecule that comprises a promoter or enhancer operable for a nucleic acid molecule encoding a protein in drug metabolism operably linked to a reporter gene, and a second nucleic acid molecule encoding an intracellular receptor or transcription factor, corresponds to canceled claim 21. New claim 84 includes the following additional phrase (claim 84 lines 8-13):

> . . . further wherein said promoter or enhancer is native to said protein involved in drug metabolism, wherein said protein involved in drug metabolism is a protein selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1; . . .

The use of a promoter or enhancer native to a protein involved in drug metabolism is supported by the specification, in particular in the Examples, such as in Example I, in which the 5' enhancer region of the CYP3A4 gene that contains the PXRE was cloned into the pGL3 vector, operably linked to a reporter gene (luciferase gene). P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1 are

included as proteins involved in drug metabolism in the specification, as described on page 28, lines 16-19 :

> The protein involved in drug metabolism can be any appropriate enzyme or transporter. Preferred enzymes involved in drug metabolism include but are not limited to P450's, transporters, glucuronoyl transferases, N-actyl transferases, glutathione transferases, p-glycoproteins and sulfo transferases. Preferred transporters include but are not limited to p-glycoprotein (MDR1).

New independent claim 84 also includes the phrase "wherein said first nucleic acid molecule, said second nucleic acid molecule, or both are stably transfected into said recombinant cell;" (claim 84 lines 21 and 22) which is supported by the specification, for example, on page 22, lines 15-18:

> The first nucleic acid molecule can be extra chromosomal, or can be integrated within the genome of the cell. When the first nucleic acid molecule is integrated within the genome of the cell, the first nucleic acid becomes stably integrated, which results in a cell having greater reliability and reproducibility than transiently transfected cells.

and on page 25, lines 14-17:

> The second nucleic acid molecule can be extra chromosomal, or can be integrated within the genome of the cell. When the second nucleic acid molecule is integrated within the genome of the cell, the second nucleic acid becomes stably integrated, which results in a cell having greater reliability and reproducibility than transiently transfected cells.

New claim 84 includes the phrase: "wherein said recombinant cell is an isolated or a cultured cell" (claim 84 line 23). Isolated and cultured cells are referred to in the definition of a "cell" on page 19 (lines 14-16): "A cell can be obtained from an organism, such as an animal or a human, and provided in primary culture or continuous cultures such as in the case of a cell line." Cultured cells, such as HepG2-derived cell lines, are also described in the Examples. New claim 108, reciting an isolated recombinant cell, and new claim 109, reciting a cultured recombinant cell, depend from independent claim 84, and are supported by the same definition on page 19 of the specification, and by the Examples.

New claims 85-107 correspond to canceled claims 22-44. New claims 110-115 correspond to canceled claims 46-51.

New claims 99, 100, and 101, corresponding to canceled claims 36, 37, and 38, now include the wording "wherein said intracellular receptor or transcription factor forms a complex with or is indirectly activated by a [drug/chemical/metabolite] . . .". Indirect activation of an intracellular receptor or transcription factor by a drug is supported by the specification, for example on page 20, lines 13-17:

> . . . when the intracellular receptor or transcription factor is in contact with a compound, or directly or indirectly activated by a compound or directly or indirectly modulated by a compound, the intracellular receptor of transcription factor can operably bind with the promoter or enhancer resulting in the expression of said reporter gene; . . .

New claim 116 corresponds to canceled claim 52 and recites a method for evaluating compounds for the property of inducing the expression of a gene encoding a protein involved in drug metabolism. Claim 116 includes the phrase (claim 116 lines 11-16):

> . . . further wherein said promoter or enhancer is native to said protein involved in drug metabolism, wherein said protein involved in drug metabolism is a protein selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1; . . .

The use of a promoter or enhancer native to a protein involved in drug metabolism in assays is supported by the specification, in particular in the Examples, such as in Example I, in which the 5' enhancer region of the CYP3A4 gene that contains the PXRE was cloned into the pGL3 vector, operably linked to a reporter gene (luciferase gene). P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1 are included as proteins involved in drug metabolism in the specification, as described on page 28, lines 16-19 :

> The protein involved in drug metabolism can be any appropriate enzyme or transporter. Preferred enzymes involved in drug metabolism include but are not limited to P450's, transporters, glucuronoyl transferases, N-actyl transferases, glutathione transferases, p-glycoproteins and sulfo transferases. Preferred transporters include but are not limited to p-glycoprotein (MDR1).

New claim 116 also includes the phrase: "wherein said recombinant cell is an isolated or a cultured cell" (claim 116 line 24). Isolated and cultured cells are referred to in the definition of a "cell" on page 19 (lines 14-16): "A cell can be obtained from an organism, such as an animal or a human, and provided in primary culture or continuous cultures such as in the case of a cell line." Cultured cells, such as HepG2-derived cell lines, are also described in the Examples. New claim 142, reciting methods using an isolated recombinant cell, and new claim 143, reciting methods using a cultured recombinant cell, depend from independent claim 116, and are supported by the same definition on page 19, and by the Examples.

New claim 117, reciting a method for evaluating compounds for the property of inducing the expression of a gene encoding a protein involved in drug metabolism, in which "said first nucleic acid molecule, said second nucleic acid molecule, or both are stably transfected into said recombinant cell;" is supported by the specification, for example, on page 22 (lines 15-18):

> The first nucleic acid molecule can be extra chromosomal, or can be integrated within the genome of the cell. When the first nucleic acid molecule is integrated within the genome of the cell, the first nucleic acid becomes stably integrated, which results in a cell having greater reliability and reproducibility than transiently transfected cells.

and on page 25 (lines 14-17):

> The second nucleic acid molecule can be extra chromosomal, or can be integrated within the genome of the cell. When the second nucleic acid molecule is integrated within the genome of the cell, the second nucleic acid becomes stably integrated, which results in a cell having greater reliability and reproducibility than transiently transfected cells.

New claims 118-141 correspond to canceled claims 53-76. New claims 144-149 correspond to canceled claims 78-83.

New claims 133, 134, and 135, corresponding to canceled claims 68, 69, and 70, now include the wording "wherein said intracellular receptor or transcription factor forms a complex with or is indirectly activated by a [drug/chemical/metabolite] . . .". Indirect activation of an intracellular receptor or transcription factor by a drug is supported by the specification, for example on page 20, lines 13-17:

> . . . when the intracellular receptor or transcription factor is in contact with a compound, or directly or indirectly activated by a compound or directly or indirectly modulated by a compound, the intracellular receptor of transcription factor can operably bind with the promoter or enhancer resulting in the expression of said reporter gene; . . .

Support for the terms compound, drug, chemical and metabolite, such as set forth in claims 99, 100, 101, 133, 134 and 135 can be found throughout the specification as filed. For example:

> A "compound" refers to any chemical, test chemical, drug, new chemical entity (NCE) or other moiety. For example, a compound can be any foreign chemical (xenobiotic) not normally present in a subject such as mammals including humans. A compound can also be an endogenous chemical that is normally present and synthesized in biological systems, such as mammals including humans. In one aspect, oxidation of compounds by enzymes generally results in a more water-soluble, easily excretable product. Examples include food additives, steroid hormones and drugs. (p. 16, ll. 20-26)
>
> "High throughput screening" refers to methods for screening for activity of compounds, such as test compounds such as drugs [...] (p. 19, ll. 27-28)
>
> Adverse reactions to therapeutic agents are a common cause of morbidity and mortality, particularly in industrialized nations where the use of such therapeutic agents is relatively common. It has been estimated that side affects from drugs are the fourth to sixth leading cause of death in hospitals in the United States (Moore and Kliewer, Toxicology 153:1-10 (2000)). A large number of these adverse reactions are due to drug interactions, a process by which the administration of one drug alters the properties of a second co-administered drug. The most common drug interactions occur when one drug either increases or decreases the effectiveness of another (Moore and Kliewer, Toxicology 153:1-10 (2000)). This modification in the pharmacological action of a drug generally stems from

alternations in the drug's metabolism. Thus, a major factor associated with drug interactions is altered metabolism. (p. 1, ll. 19-28)

Prolonged exposure to drugs can lead to an increased expression of specific p450s that can augment the metabolism and clearance of therapeutic drugs. CYP3A4 activity is enhanced by a range of diverse chemicals and its induced expression is the cause of many drug interactions. Several of the most efficacious inducers of CYP3A4 expression are commonly used drugs such as the gluccocorticoid dexamethasone, the anticonvulsant phenobarbital, the antibiotic rifampicin and the antimycotic clotrimazone [...] (p. 2, ll. 20-25)

A "sulfo transferase" refers to polypeptides or proteins such as enzymes that catalyze the sulfation of structurally diverse xenobiotics including drugs and endogenous compounds. (p. 17, ll. 22-23)

In one aspect of the present invention, the intracellular receptor or transcription factor forms a complex with a xenobiotic such as a drug, chemical or metabolite thereof and directly or indirectly produces transcriptional activation of a gene encoding a protein involved in drug metabolism. (p. 30, ll. 2-5)

For example, a compound can be any foreign chemical (xenobiotic) not normally present in a subject such as mammals including humans. A compound can also be an endogenous chemical that is normally present and synthesized in biological systems, such as mammals including humans. (p. 16, ll. 19-24)

The present invention provides improved cells and methods for identifying compounds that alter protein expression, such as chemicals or drugs. (p. 20, ll. 5-6)

The present invention provides improved cells and methods for identifying compounds that alter protein expression, such as xenobiotics, endobiotics, chemicals or drugs. (p. 60, ll. 6-7)

A "drug metabolizing enzyme" refers to enzyme proteins that catalyze the covalent modification of xenobiotics such as drugs that are foreign to the host. Such covalent modifications can be any, but are preferably oxidation or conjugation reactions. The oxidation reactions generally result in water soluble metabolites or metabolites with increased water solubility. (p. 15, ll. 3-7)

Sulfate conjugation generally results in a detoxification producing water soluble metabolites. (p. 17, ll. 26-27)

Preferred transporters include but are not limited to p-glycoprotein (MDR1). This protein transports drug metabolites out of a cell and can influence the rate of drug metabolism by a cell. (p. 28, ll. 19-21)

THE CLAIMED INVENTION COMPLIES WITH 35 U.S.C. 101

The Examiner has rejected claims 21-51 under 35 U.S.C. 101 as being directed to nonstatutory subject matter. In order to expedite prosecution of the application, Applicant has canceled claims 21-51. New independent claim 84, which corresponds to canceled independent claim 21, includes the phrase "wherein said recombinant cell is an isolated cell or a cultured cell" (line 23 of claim 84). New claims 85-115 depend from claim 84. Applicant therefore respectfully requests that the rejection be withdrawn.

THE CLAIMED INVENTION COMPLIES WITH 35 U.S.C. 112, FIRST PARAGRAPH

The Examiner rejected claims 21-83 under 35 U.S.C. 112, first paragraph, as allegedly nonenabling. The Examiner states that the specification is enabling for cells that are isolated and/or cultured. Applicant has canceled claims 21-83. To expedite the allowance of claims, Applicant has submitted new independent claims 84 and 116 that include the phrase "wherein said recombinant cell is an isolated cell or a cultured cell" (line 23 of claim 84; line 22 of claim 116). Claims 85-115 depend from claim 84 and claims 117-149 depend from claim 116. Applicant therefore respectfully requests that this rejection be withdrawn.

THE CLAIMED INVENTION COMPLIES WITH 35 U.S.C. 112, SECOND PARAGRAPH

The Examiner rejected claims 21-83 under 35 U.S.C. 112, second paragraph, as allegedly being vague and indefinite due to the lack of clarity of the promoter or enhancer encompassed by the claims. To expedite allowance of claims, applicant has canceled claims 21-83. New independent claims 84 and 116 include the following: "further wherein said promoter or enhancer is native to said protein involved in drug metabolism, wherein said protein involved in drug metabolism is a protein selected from the group consisteing of P450 proteins, glucuronosyl transferases, N-acetyltranssferases, P-glycoproteins, glutathione transferases, sulfo transferases, and MDR1;" (lines 8-13 of claim 84; lines 10-14 of claim 116). Claims 85-115 depend from

claim 84 and claims 117-149 depend from claim 116. Claims 84-149 comply with 35 U.S.C. 112, second paragraph. Applicant therefore respectfully requests that the rejection be withdrawn.

The Examiner has further asserted that claims 21, 36-38, and 52 are allegedly vague and indefinite for use of the phrase "proteins involved in drug metabolism". The examiner alleges that claims 22-51 and 53-83 are also indefinite due to their dependency from claims 21 and 52. To expedite allowance of claims, applicant has canceled claims 21-83. New claims 84 (corresponding to canceled claim 21), 99-101 (corresponding to canceled claims 36-38) and 116 (corresponding to canceled claim 52) include the following phrase: "wherein said protein involved in drug metabolism is a protein selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, P-glycoproteins, glutathione transferases, sulfo transferases, and MDR1;" (lines 9-13 of claim 84; lines 11-14 of claim 116). New claims 85-115 depend from claim 84, and claims 117-149 depend from claim 116. Thus, claims 84-149 comply with 35 U.S.C. 112, second paragraph. Applicant therefore respectfully requests that the rejection be withdrawn.

The Examiner has also rejected claims 21 and 52 as allegedly vague and indefinite in the reference to the compound in lines 10 and 14 of claim 21, and in lines 14 and 18 of claim 52. Claims 21 and 52 have been canceled. In new independent claim 84, the first recitation of compound in lines 16 and 17 of amended claim 21, reads: " a compound that induces the expression of said protein involved in drug metabolism" and the subsequent reference, in line 24 of the claim, is to "said compound". New independent claim 116, corresponding to canceled claim 52, also recites, in lines 17–18 "a compound that induces the expression of said protein involved in drug metabolism" and later refers in line 23 of the claim to "said compound". The compound referred to in the claim is clear and definite, and Applicant therefore respectfully requests that the rejection be withdrawn.

THE PRIOR ART FAILS TO ANTICIPATE THE CLAIMED INVENTION UNDER 35 U.S.C. 102 (b)

Applicant's claimed invention is novel over prior art prior to amendment. To expedite the allowance of claims, however, Applicant has canceled claims 21-83 and submitted new claims 84-149. Applicant does so without prejudice to pursuing the original claims or related claims in another application.

The Examiner rejected claims 21, 22, 29-34, 36-40, 42-45, 47, and 48 under 35 U.S.C. 102(b) as allegedly being anticipated by Honkakoski et al. (*Mol. Cell. Biol.*, Oct. 1998). New independent claim 84, corresponding to canceled independent claim 21, recites a recombinant cell comprising a first nucleic acid molecule comprising a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reported gene, and a second nucleic acid molecule comprising an intracellular receptor or transcription factor, "wherein said first nucleic acid molecule, said second nucleic acid molecule, or both, are stably transfected into said recombinant cell". Honkakoski et al. does not teach recombinant cells stably transfected with one or both of the recited nucleic acid molecules. Thus, claim 84, and claims 85, 92-97, 99-103, 105-107, 111, and 112 that are dependent on claim 84 and correspond to canceled claims 22, 29-34, 36-40, 42-44, 47, and 48, respectively, are not anticipated by Honkakoski et al. Thus Honkakoski et al. does not anticipate the claims and applicant respectfully requests that the rejection be withdrawn.

The Examiner has also rejected claims 52-54, 61-66, 68-72, 74-77, 79, and 80 under 35 U.S.C. 102(b) as allegedly being anticipated by Honkakoski et al. (*Mol. Cell. Biol.*, Oct. 1998). These claims have been canceled. New claims 118, 119, 126-131, 133-137, 139-141, 145, and 146 are dependent on new independent claim 116, and correspond to canceled claims 53, 54, 61-66, 68-72, 74-76, 79, and 80, respectively, that were dependent on canceled independent claim 52.

Applicants do not agree that Honkakoski teaches *a method for evaluating compounds* for the property of inducing the expression of a gene encoding a protein involved in drug metabolism that comprises contacting a test compound with a recombinant cell comprising a first nucleic acid molecule comprising a promoter or enhancer operable for a nucleic acid molecule encoding a

protein involved in drug metabolism operably linked to a reported gene, and a second nucleic acid molecule comprising an intracellular receptor or transcription factor, and detecting expression of the reporter gene. In contrast, Honkakoski refers to the use of promoter or enhancer fragments (specifically, PBREM sequences) linked to a reporter gene (CAT) *to identify orphan receptors* (CAR, RXR) *that can bind the promoter or enhancer fragments* to regulate gene expression in response to a particular modulating compound. Thus, applicants respectfully request that the rejection be withdrawn.

THE PRIOR ART FAILS TO ANTICIPATE THE CLAIMED INVENTION UNDER 35 U.S.C. 102 (e)

Applicant's claimed invention is novel over prior art prior to amendment. To expedite the allowance of the application, however, Applicant has canceled all pending claims and provided new claims. Applicant does so without prejudice to pursuing the original claims or related claims in another application.

The Examiner rejected Claims 21, 29, 31, 36, 41, 44-47, 52, and 53 under 35 U.S.C. 102(e) as allegedly being anticipated by Lohray et al. (U.S. Patent No. 6,054,453). New claims 84, 92, 94, 99, 104, 107, 110, 111, 116, and 118 correspond to canceled claims 21, 29, 31, 36, 41, 44, 46, 47, 52, and 53, respectively. New independent claims 84 and 116 refer to a cell comprising first and second nucleic acid molecules. The first nucleic acid molecule comprises a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, wherein "said promoter or enhancer is native to said protein involved in drug metabolism, wherein said protein involved in drug metabolism is a protein selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1".

In contrast, Lohray et al. refers to a cell comprising two plasmids or nucleic acid molecules wherein the first nucleic acid molecule taught by Lohray et al. comprises a GAL4 promoter, which is not "a promoter or enhancer native to a protein involved in drug metabolism

selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1". Thus, the reference does not teach each and every element of the claimed invention and thus does not anticipate the claimed invention. Applicant therefore respectfully requests that this rejection be withdrawn.

APPLICANT'S CLAIMED INVENTION IS NOT OBVIOUS UNDER 35 U.S.C. § 103(A) IN VIEW OF THE REFERENCES CITED BY THE EXAMINER

Applicant's claimed invention is non-obvious over the prior art prior to amendment. To expedite the allowance of the application, however, Applicant has canceled all pending claims and submitted new claims. Applicant does so without prejudice to pursuing the original claims in another application.

The Examiner rejected claims 21-34, 36-40, 42-62, 64-66, 68-71, and 74-83 under 35 U.S.C. 103(a) as allegedly being unpatentable over Honkakoski et al., in view of Iyer et al. (Eur. J. Cancer 34: 1493-1499 (1998)) and Windmill et al. (Mutation Research 376: 153-160(1997)). New independent claim 84 (which corresponds to canceled independent claim 21) recites a recombinant cell comprising a first nucleic acid molecule comprising a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, and a second nucleic acid molecule comprising an intracellular receptor or transcription factor, "wherein said first nucleic acid molecule, said second nucleic acid molecule, or both, are stably transfected into said recombinant cell". Honkakoski et al. demonstrates the use of cells transiently transfected with nucleic acid constructs. Iyer et al. describes drug metabolizing enzymes and Windmill et al. describes organs and tissues in which genes for drug metabolizing enzymes are expressed. However, the cited references alone or in combination do not teach or suggest the use of cells stably transfected with at least one of the recited nucleic acid constructs, and therefore do not teach or suggest each and every element of independent claim 84. Claim 84

and claims that are dependent on claim 84 (such as claims 85-97, 99-103, 105-107, 110-115, corresponding to canceled claims 22-34, 36-40, 42-44, and 46-51) are not rendered obvious by Honkakoski et al., Iyer et al., and Windmill et al. Applicant therefore respectfully requests that the rejection be withdrawn.

As detailed in the section immediately above concerning the U.S.C. 102(e) rejection, Honkakoski et al. does not teach or suggest a method for *evaluating compounds* for the property of inducing the expression of a gene encoding a protein involved in drug metabolism. Iyer et al. and Windmill et al. also do not teach or suggest, alone, together, or in combination with Honkakoski et al., a method for evaluating compounds for the property of inducing the expression of a gene encoding a protein involved in drug metabolism. Thus, Iyer et al. and Windmill et al. do not make up for the deficiencies of Honkakoski et al. Therefore all of the elements of independent claim 116, and dependent claims 118-127, 129-131, 133-136, 139-141, and 144-149, corresponding to canceled claims 53-62, 64-66, 68-71, 74-76, and 78-83, are not taught or suggested by the cited references, and Applicant requests that the rejection be withdrawn.

The Examiner has also rejected claims 22, 32-35, 39, 42, and 43 under 35 U.S.C. 103(a) as allegedly being unpatentable over Lohray et al. in view of Lusky et al. (U.S. Patent No. 6,262,118), Foulkes et al. (U.S. Patent No. 5,976,793), Boeke et al. (U.S. Patent No. 5,840,579), Klein et al. (U.S. Patent No. 6,255,059), and Sherr et al. (U.S. Patent No. 6,303,772).

To expedite prosecution of the application, applicant has canceled independent claim 21 and provided independent claim 84 that includes a first nucleic acid molecule that comprises a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, wherein "said promoter or enhancer is native to said protein involved in drug metabolism, wherein said protein involved in drug metabolism is a protein selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1".. . Lohray refers to a cell comprising two plasmids or nucleic acid molecules wherein the first

nucleic acid molecule comprises a GAL4 promoter, which is not a promoter or enhancer native to a protein involved in drug metabolism selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1". Neither Luskey et al., Foulkes et al. Boeke et al., Klein et al., or Sherr et al., alone, together, or in combination with Lohray, teach or suggest a cell transfected with a construct that comprises a reporter gene linked to a "promoter or enhancer native to said protein involved in drug metabolism, wherein said protein involved in drug metabolism is a protein selected from the group consisting of P450 proteins, glucuronosyl transferases, N-acetyltransferases, p-glycoproteins, glutathione transferases, sulfo transferases, and MDR1".. Thus, Luskey et al., Foulkes et al. Boeke et al., Klein et al., and Sherr et al. do not make up for the deficiencies of Lohray et al. The cited references, either alone or in combination, fail to teach or suggest all elements of independent claim 84 and dependent claims 85, 95-98, 102, 105, and 106, and thus fail to render the claimed invention obvious. Accordingly, Applicant respectfully requests that the rejection be withdrawn.

INFORMATION DISCLOSURE STATEMENT FILED WITH USPTO ON SEPTEMBER 30, 2003

Applicant notes that an Information Disclosure Statement was filed in the subject patent application on September 30, 2003. A copy of that document is provided for the examiner's convenience.

Applicants respectfully submit that the claims are ready for examination and in condition for allowance.

Respectfully submitted,

Date: Oct 20, 2003

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Patent
Docket Number: PUR-00114.P.1.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
Raucy	Examiner: Monika Sheinberg
Application No.: 09/832,621	Art Unit: 1634
Filed: April 11, 2001	
For: COMPOSITIONS AND METHODS FOR INDUCTION OF PROTEINS INVOLVED IN XENOBIOTIC METABOLISM	

Commissioner for Patents
Alexandria VA 22313

Sir:

INFORMATION DISCLOSURE STATEMENT #3

Applicant respectfully submits this Information Disclosure Statement (IDS) after the mailing of a First Office Action on the merits under 37 C.F.R. §1.97(a)(3).

Applicant also submits a Form 1449, volumes of references cited on Applicant's Form 1449, and a check for $180.00 to cover the IDS fee.

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Please apply any charges not covered, or any credits, to Deposit Account number 501321 in the name of David R. Preston & Associates, having Customer Number 24232.

Respectfully submitted,

Date: Sep 30, 2003

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)	Docket Number: PUR-00114.P.1.1	Application Number: 09/832,621
	Applicant: Raucy	
	Filing Date: April 11, 2001	Group Art Unit: 1634

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	P1	5,071,773	12/10/91	Evans et al.			
	P2	5,298,429	3/29/94	Evans et al.			
	P3	5,639,616	6/17/97	Liao et al.			
	P4	2002/022599	2/21/02	Synold et al.			
	P5	2002/0150915	10/17/02	Berkenstam et al.			
	P6	2002/0168623	11/14/02	Raucy			
	P7	2003/0064430	4/03/03	Evans et al.			

Examiner Signature		Date Considered	

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FOREIGN PATENT DOCUMENTS								
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	Translation	
							YES	NO
	F1	EP 0 644 267 A2	7/20/94	EPO				
	F2	WO 88/03168	5/5/88	PCT				
	F3	WO 94/27557	12/8/94	PCT				
	F4	WO 99/61622	12/2/99	PCT				
	F5	WO 01/20026 A2	3/22/01	PCT				
	F6	WO 01/71361 A1	9/27/01	PCT				
	F7	WO 01/97856 A2	12/27/01	PCT				
	F8	WO 02/24918 A1	3/28/02	PCT				
	F9	WO 02/36784 A1	5/10/02	PCT				
	F10	WO 02/088305 A2	11/7/02	PCT				
	F11	WO 02/094865 A1	11/28/02	PCT				
	F12	WO 02/095652 A1	11/28/02	PCT				

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
EXAMINER INITIALS		CITATION
	D1	Barwick, Mol. Pharmacol., 50:10-16 (1996).
	D2	Dogra et al., Clinical Pharmacology and Physiology, 25: 1-9 (1998).
	D3	Chen et al., Mol. Pharmacol., 64:316-324 (2003).
	D4	Cui et al., Journal of Pharmacology and Toxicological Methods, 47: 143-151 (2002).
	D5	Ferguson et al., Mol. Pharmacol. 62(3): 737-746 (2002).
	D6	Gonzalez et al., DNA, 7(2): 79-86 (1988).
	D7	Hakkola et al., Critical Reviews in Toxicology, 28(1): 35-72 (1998)
	D8	Hashimoto et al., Eur. J. Biochem., 218: 585-595 (1993).
	D9	Honkakoski et al., Ann. Med. 35(3): 172-182 (2003).
	D10	Kliewer et al., Cell, 92:73-82 (1998).
	D11	Kolars et al., Pharmacogenetics 4: 247-259 (1994).
	D12	Kovaleva et al., Biochemical and Biophysical. Research Communications 221: 129-132 (1996).
	D13	Moore et al., Molecular Endocrinology 16(5):977-986 (2002).
	D14	Ogg et al., Eur. J. of Drug Metabolism and Pharmacokinetics 22(4): 311-313 (1997).
	D15	Sakai and Takigami, Ind. Health 41: 205-214 (2003).
	D16	Smith et al., Xenobiotica, 28(12): 1129-1165 (1998).
	D17	Sonoda et al., Proc. Natl. Acad. Sci USA 99(21): 13801-13806 (2002).
	D18	Sulston and Waterston, Genome Res., 8(11): 1097-1108 (1998).
	D19	Xie et al., Proc Natl. Acad. Sci. USA 100(7): 4150-4155 (2003).
	D20	Yanagida et al., Molecular and Cellular Biology, 10(4): 1470-1475 (1990).
	D21	Yueh et al., J of Biological Chemistry 278(17): 15001-15006 (2003).

Examiner Signature		Date Considered	

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